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Pabst Patent Group LLP
1545 PEACHTREE STREET NE
SUITE 320
ATLANTA, GA 30309

EXAMINER	
FLOOD, MICHELE C	
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte AVRAHAM J. DOMB
and
JOSEPH SIMCHA WOLNERMAN,
Appellants[1]

Appeal 2008-003664
Application 10/083,413
Technology Center 1600

Decided: May 20, 2010

Before CAROL A. SPIEGEL, DEMETRA J. MILLS, and
STEPHEN WALSH, *Administrative Patent Judges*.

SPIEGEL, *Administrative Patent Judge*.

DECISION ON APPEAL

Appellants appeal under 35 U.S.C. § 134(a) from an Examiner's final rejection of all pending claims, claims 1-4, 6-12, 14-17, 19-26, and 38 (App.

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[1] The real party in interest is AXIOMEDIC, INC. (Appeal Brief filed 19 October 2006 ("App. Br.") at 2).

Br. 2). Oral arguments were held May 11, 2010. We have jurisdiction under 35 U.S.C. § 134. We AFFIRM-IN-PART.

I. Statement of the Case

The subject matter on appeal is directed to a solid, self-adhesive composition for topical application that adheres to oral mucosal tissue comprising (a) a therapeutically effective amount of at least one herbal or homeopathic active agent and (b) a pharmaceutically acceptable solid bioadhesive carrier in an amount from about 40 to 99 percent based on the weight of the whole composition (Spec.[2] 10, ¶ 5). Claim 1 is the sole independent claim on appeal and reads (App. Br. 18):

> 1. A solid, self-bioadhesive composition for topical application that adheres to oral mucosal tissue comprising:
>
> (a) a therapeutically effective amount of at least one herbal active agent wherein the herbal active agent is selected from the group consisting of bioactive herbs, herbal extracts, tinctures, essential oils, and mixtures thereof, and
>
> (b) a pharmaceutically acceptable solid bioadhesive carrier, comprising a mucoadhesive synthetic polycarboxylic acid polymer, in an amount from about 40 to 99 percent based on the weight of the whole composition in a form suitable for administration and adhesion to the oral mucosa.

The bioadhesive carrier of claim 1 may be crosslinked synthetic polycarboxylic acid polymers and mixtures thereof (claim 22), especially polyacrylic acid polymers crosslinked with a polyalkenyl polyether,

[2] "Spec." refers to the Specification of application 10/083,413 ("the 413 application").

carboxymethylcellulose, hydroxymethylcellulose, and mixtures thereof (claim 26) (App. Br. 21).

In one claimed embodiment, the composition of claim 1 is formed into a disc 2 to 15 mm diameter and 0.4 to 2.3 mm thick which adheres to the oral mucosa tissue for at least 30 minutes (claim 2) (App. Br. 18). In another claimed embodiment, the composition of claim 1 has a surface area ranging from about 0.4 to about 3 cm^2 (claim 38) (App. Br. 22).

Other embodiments claim a composition wherein the herbal active agent is an essential oil (claims 7-8), at least one monoterpene with three unsaturations (claims 9 and 11), or an essential oil which is a natural or synthetic mixture consisting of limonene and at least one myrcene, a-pinene, b-pinene, and sabinene characterized in that at least 60% by weight of the mixture is limonene (claim 10); or, a composition comprising $MgBr_2$, NaCl, and/or KCl (claim 12) or carnallite or a salt of carnallite (claim 14).

The Examiner has rejected

(A) claims 1-3, 15-17, 22-24, 26, and 38 as anticipated under 35 U.S.C. § 102(b) by Nagai[3] (Ans.[4] 7);

(B) claims 1-4, 6, 15-17, 22-24, and 38 as anticipated under 35 U.S.C. § 102(b) by Inoue[5] (Ans. 3-7); and,

(C) claims 1-4, 6-12, 15-17, 19, 22-24, and 38 as obvious under 35 U.S.C. § 103(a) over Inoue in view of Iyer[6] and Friedman[7] (Ans. 7-12). The

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[3] U.S. Patent 4,226,848, *Method and Preparation for Administration to the Mucosa of the Oral or Nasal Cavity*, issued 7 October 1980, to Nagai et al. ("Nagai").
[4] Examiner's Answer mailed 14 March 2007 ("Ans.").
[5] U.S. Patent 4,772,470, *Oral Bandage and Oral Preparations*, issued 20 September 1988, to Inoue et al. ("Inoue").

Examiner also relies on Lawless[8] and Odian[9] as evidence of inherency (Ans. 8, 14, and 18).

Notably, the Examiner has not rejected claims 14, 20, 21, and 25.

In rejection (A), the Examiner found that Nagai described the subject matter of claims 1-3, 15-17, 22-24, 26, 27, and 38 (Ans. 9). Appellants acknowledge that Nagai describes compositions comprising a mucosa-adhesive polymeric matrix comprising about 50% to about 95% by weight cellulose ether and about 50 to about 5% by weight homo- or co-polymer of acrylic acid as well as a pharmaceutically effective amount of a medicament dispersed in the matrix (App. Br. 9). However, Appellants argue that none of the medicaments described in Nagai are bioactive herbs, herbal extracts, tinctures, essential oils, or mixtures thereof as required by claim 1 (*id.*). Appellants further argue that there is no disclosure in Nagai of crosslinked matrix polymers as required by claims 22 and 26 (*id.* at 9-10).

Based on Appellants' patentability arguments, we decide rejection (A) on the basis of claims 1 and 22. 37 C.F.R. § 41.37(c)(1)(vii). Thus, at issue in rejection (A) is whether Nagai describes a medicament selected from the group of bioactive herbs, herbal extracts, tinctures, essential oils, or mixtures

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[6] U.S. Patent 5,939,050, *Antimicrobial Compositions*, issued 17 August 1999, to Iyer et al. ("Iyer").

[7] U.S. Patent 6,197,305 B1, *Anti-Fungal Compositions with Prolonged Activity*, issued 6 March 2001, based on application 09/002,925, filed 5 January 1998, to Friedman et al. ("Friedman").

[8] Julia Lawless, THE ILLUSTRATED ENCYCLOPEDIA OF ESSENTIAL OILS: THE COMPLETE GUIDE TO THE USE OF OILS IN AROMATHERAPY AND HERBALISM, Element Books 1995, pp. 115, 120, 123, 134, 139-141, 196, and 197 ("Lawless").

[9] George Odian, PRINCIPLES OF POLYMERIZATION, Third Edition, John Wiley & Sons, Inc. 1991, pp. 520-521 ("Odian").

thereof recited in claim 1; and, if so, whether the polymers in the polymeric matrix of Nagai are crosslinked as required by claim 22.

In rejection (B), the Examiner found that Inoue described the subject matter of claims 1-4, 6, 15-17, 22-24, and 38 (Ans. 3-6). Appellants acknowledge that Inoue describes an oral bandage with a soft adhesive film comprising a mixture of a polycarboxylic acid and/or a polycarboxylic acid anhydride and a vinyl acetate polymer as well as a topical drug incorporated into the film (App. Br. 7). However, Appellants argue that Inoue does not describe a composition comprising a bioadhesive carrier in amount from about 40 to 99% by weight based on the total weight of Inoue's composition as required by claim 1 (*id.* at 7). Appellants further argue that Inoue does not disclose or suggest compositions having the surface area specified in claim 38 or formed into discs having the diameters and thicknesses specified in claims 2 and 3 (*id.* at 8). Finally, Appellants argue that Inoue does not describe crosslinked matrix polymers as required by claim 22[10] (*id.*).

Based on Appellants' patentability arguments, we decide rejection (B) on the basis of claims 1, 2, 22, and 38. 37 C.F.R. § 41.37(c)(1)(vii). Thus, at issue in rejection (B) is whether Inoue describes a composition comprising a bioadhesive carrier in amount of about 40 to 99 weight% based on the total weight of the composition as required by claim 1; and, if so, whether Inoue describes compositions (a) having a surface area from about 0.4 to about 3 cm^2 as required by claim 38, (b) formed into a disc of 2 to 15 mm diameter and 0.4 to 2.3 mm thickness as required by claim 2, and/or (c) having a carrier comprising crosslinked polymers as required by claim 22.

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[10] Although Appellants included claim 26 in this argument, claim 26 has not been rejected under § 102(b) as anticipated by Inoue.

In rejection (C), the Examiner found that Inoue described the claimed invention but for a composition wherein the herbal active agent is an essential oil (claims 7-8), at least one monoterpene with three unsaturations (claim 9), or an essential oil which is a natural or synthetic mixture consisting of limonene and at least one myrcene, a-pinene, b-pinene, and sabinene characterized in that at least 60% by weight of the mixture is limonene (claim 10); or, a composition comprising $MgBr_2$, NaCl, and/or KCl (claim 12) (Ans. 7-9 and 17). The Examiner found that Iyer teaches that various herbal active agents, including essential plant oils, e.g., citronella or lemon oil, and herbal extracts, are useful in oral hygiene products as antimicrobial agents (*id.* at 9). The Examiner also found that Friedman teaches a combination of an herbal extract and an essential oil, such as a cinnamon, citronella, lemon, or tea-tree oil, that exerts antibacterial, anti-inflammatory, and antifungal activity on mucosal membranes (*id.* at 9-10). The Examiner concluded that it would have been obvious to add at least an essential oil, such as lemon oil, as taught by Iyer and Friedman to the active ingredients in the composition of Inoue to provide an oral antimicrobial composition (*id.* at 10-11). The Examiner relied on Lawless to establish that lemon oil comprises 70% limonene, myrcene, pinenes, and sabinene (*id.* at 11). The Examiner also concluded that since each of the references indicated that the various proportions and amounts of ingredients used are result variables, one of ordinary skill in the art would have routinely optimized their concentration for the composition's intended use (*id.* at 11-12).

Appellants reiterate their argument that Inoue does not describe the subject matter of claims 1, 2, 3, 22, and 38 set forth in rejection (B) (App. Br.

12-15). As to rejected claims 7-12 and 19, Appellants argue that none of Iyer, Friedman, and Lawless teach or suggest a composition comprising a bioadhesive carrier in amount of about 40 to 99 weight% based on the total weight of the composition as required by claim 1 and, therefore, claims 7-12 and 19 are not obvious over the combined teachings of Inoue, Iyer, Friedman, and Lawless (App. Br. 15-16). Appellants further argue that Inoue fails to teach or suggest a composition comprising $MgBr_2$, NaCl, and/or KCl as required by claim 12 or a composition containing carnallite or a salt thereof as required by claim 19 (*id.* at 15). Appellants also argue that there is no motivation to combine the teachings of the applied references (Reply Br.[11] 13).

Based on Appellants' patentability arguments, we decide rejection (C) on the basis of claims 1, 2, 7, 12, 19, 22, and 38. 37 C.F.R. § 41.37(c)(1)(vii). Since the issues with regard to claims 1, 2, 22, and 38 are essentially the same as raised in rejection (B), the new issues before us in rejection (C) are (i) whether the Examiner has established a sufficient basis for combining the teachings of the applied references, (ii) whether Appellants' proffered showing of unexpected results is sufficient to establish nonobviousness, and (iii) whether the applied references teach or suggest a composition comprising the further ingredients of claims 12 ($MgBr_2$, NaCl, and/or KCl) or 19 (carnallite or a salt thereof).

II. Findings of Fact

The following findings of fact are supported by a preponderance of the evidence of record.

A. The 413 application

[11] Reply to Examiner's Answer filed 14 May 2007 ("Reply. Br.").

[1] According to the Specification,

> The term "bioadhesive" as used herein means an adhesive which attaches and preferably strongly attaches to mucosal tissue upon hydration. Indeed, to qualify as a bioadhesive, a substance must be capable of maintaining adhesion in moist or wet in-vivo environments. The final composition of the present invention is "self-adhesive" in that it attaches to the site of interest without the need to reinforce its attachment by way of another adhesive which is applied to a backing. [Spec. ¶ bridging 12-13].

[2] Suitable adhesive carriers include nontoxic polymers containing carboxylic acid, such as copolymers of acrylic or methacrylic acid, copolymers of maleic acid, polysaccharides, and cellulose and cellulose derivatives (Spec. 12, ¶ 2; 13, ¶¶ 2-3).

[3] A particularly preferred carrier contains "mixtures of slightly crosslinked polyacrylic acid, i.e. Carbopol 940, 934, 974, and the like, carboxymethyl cellulose and hydroxypropylmethyl cellulose (HPMC)" (Spec. 12, ¶ 2).

[4] According to the Specification, Carbopol 934, 934P, 974, 940, and 941 are "polyacrylic acid polymers lightly crosslinked with a polyalkenyl polyether" which are commercially available from B.F. Goodrich (Spec. 13, ¶ 1).

B. Nagai

[5] Nagai describes oral or nasal mucosa-adhesive preparations comprising a polymeric matrix containing (a) about 50 to about 95% by weight of a cellulose ether and about 50 to about 5% by weight of a homo- or copolymer of acrylic acid or a pharmaceutically acceptable

salt thereof; and (b) dispersed therein, a pharmaceutically effective amount of a medicament (Nagai, col. 2, l. 67-col. 3, l. 10).

[6] Exemplary medicaments include anti-inflammatory steroids, such as hydrocortisone and dexamethasone, cardiac tonics such as digitalis and digoxin, and topical anaesthetics, such as benzocaine, which can be used singly or in combination (Nagai, col. 5, l. 58-col. 6, l. 19).

[7] Exemplary matrices comprise mixtures of hydroxypropyl cellulose and Carbopol 934 (Nagai, col. 13, ll. 47-55; col. 14, ll. 53-55).

C. Inoue

[8] Inoue describes an oral bandage for administering an active agent to the oral mucosa comprising (i) a "compatible" mixture of a polycarboxylic acid and/or a polycarboxylic acid anhydride (collectively "polycarboxylic acids") and a vinyl acetate polymer (hereinafter "polyvinyl acetate"), and (ii) a topical drug (Inoue, col. 2, ll. 24-38; col. 3, ll. 8-15).

[9] The polycarboxylic acids and polyvinyl acetate are "uniformly dissolved in each other without forming small individual regions due to phase separation" (Inoue, col. 2, ll. 32-38) and can be formed into a thin and soft film which exerts strong adhesion for an extended period of time without degrading, generally 3 to 4 hours or longer (*id.* at col. 2, l. 60-col. 3, l. 2; col. 11, ll. 2-10).

[10] The ability of Inoue's mixture of polycarboxylic acids and polyvinyl acetate to uniformly swell without degradation even when immersed in water for a considerably long period of time is present whether or not a neutralizing basic substance, such as zinc oxide or sodium

acetate, is also present in the mixture (Inoue, col. 4, ll. 3-11; col. 5, ll. 13-18).

[11] The "compatibility" of Inoue's mixture is defined by a dissolution ratio of polycarboxylic acids of 40 wt. % or less or, in the presence of a neutralizing salt, a ratio of 50 wt. % or less (Inoue, col. 4, ll. 21-31).

[12] Inoue believes that

> the polycarboxylic acids contribute to adhesiveness to the wet mucosa and the polyvinyl acetate contributes to water resistance in a compatible mixture thereof, thus functioning in harmony to show adhesion of long duration (Inoue, col. 5, ll. 3-8).

[13] Typically, the topical drug is added directly or in the form of a solution to a solution of polycarboxylic acids and polyvinyl acetate, and the resulting solution is cast onto a thin film, e.g., polyethylene-laminated paper, subjected to releasability-imparting treatment, dried, and peeled off to produce an oral bandage comprising a drug-incorporated adhesive film (Inoue, col. 5, l. 66-col. 6, l 5; col. 7, l. 64-col. 8, l. 11; Examples 7-9 and 20 to 37).

[14] The thickness of the resulting film is preferably from 5 to 100 μm because it is difficult to obtain sufficient adhesion with a film less than 5 μm, while a film thicker than 100 μm feels foreign and has impaired softness (Inoue, col. 8, ll. 11-17).

[15] While Inoue's oral bandage "may solely comprise the adhesive film," it may further comprise a soft film support in combination, i.e., a "composite film" (Inoue, col. 8, ll. 30-33).

[16] The film support is typically a substantially water impermeable plastic film having a thickness from 10 to 100 μm (Inoue, col. 8, ll. 45-55).

[17] Exemplary topical drugs include steroids, e.g., dexamethasone, anti-inflammatories, e.g., Lithospermi Radix extract, and analgesics, e.g., lidocaine (Inoue, col. 9, ll. 6-53).

[18] The amount of incorporated topical drug usually ranges from 0.0001 to 35 wt. %, based on the preparation (Inoue, col. 9, ll. 54-60).

D. Iyer

[19] Iyer teaches antibacterial compositions for use in oral hygiene products, e.g., dentrifices and mouth rinses, comprising two agents, A and B, one of which when in combination the other is able to inhibit or prevent bacterial growth at a concentration lower than the concentration needed in the absence of the other (Iyer, col. 3, ll. 5-10 and ll. 47-51).

[20] The composition can be used by contacting a surface where inhibition of bacterial growth is desired with the composition (Iyer, col. 3, ll. 53-55; col. 7, ll. 16-18).

[21] Suitable agents A and B include cedarwood oil, citronella oil, *Glycyrrhiza glabra* extract (licorice root extract), and lemon oil (Iyer, col. 3, ll. 11-27; col. 4, ll. 34-36).

[22] Table 3 illustrates how combining various agent Bs, including citronella oil (CTR1), lemon oil (LMO1), and *Glycyrrhiza glabra* extract, a specific agent A, cedarwood oil (RC1), decreases the minimum inhibitory concentration ("MIC") of cedarwood oil alone (Iyer, col. 10, ll. 13-34).

[23] Suitable amounts of each agent range from about 0.001 wt. % to about 5.0 wt. % based on the total weight of composition containing the agents (Iyer, col. 7. ll. 12-15).

E. Friedman

[24] Friedman discloses a composition comprising specific combinations of essential oils and herbal extracts for topical application to mucosal membranes, e.g., the oral cavity, for treating microbial infections caused by bacteria or fungi (Friedman, col. 1, ll. 6-21; col. 2, ll. 20-28; col. 3, ll. 8-17; col. 4, ll. 30-36).

[25] Preferred essential oils include cinnamon oil, citronella oil, lemon oil, and tea-tree oil, preferably from about 0.2 to about 2.0 wt. % (Friedman, col. 2, ll. 37-49).

[26] Preferred herbal extracts include Glycerrhiza extracts, preferably from about 1 to about 10 wt. % (Friedman, col. 2, ll. 50-59).

[27] Compositions for local oral administration may be in the form of toothpastes, creams, ointments, gels, solutions, or chewable tablets (Friedman col. 9, l. 66-col. 10, l. 4).

F. Lawless

[28] According to Lawless, the principal components of essential lemon oil are limonene (approximately 70%), terpinene, pinenes, sabinene, myrcene, citral, linalool, geraniol, octanol, nonanol, citronellal, and bergamontene (Lawless 120).

G. Odian

[29] According to Odian,

> Neutralization of ethylene copolymers containing up to 5-10% acrylic or methacrylic copolymer with a metal salt such as the acetate or oxide of zinc, sodium, magnesium, barium, or aluminum yields products referred to as *ionomers* … Ionomers act like reversibly crosslinked thermoplastics as a result of microphase separation between ionic metal carboxylate and

> nonpolar hydrocarbon segments. The behavior is similar to the physical crosslinking in thermoplastic elastomers … (Odian 520).

III. Discussion

A. Legal principles

Anticipation requires that a prior art reference describe every limitation in a claim either explicitly or inherently. *In re Schreiber*, 128 F.3d 1473, 1477 (Fed. Cir. 1997). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re Oelrich*, 666 F.2d 578, 581 (CCPA 1981). Nonetheless, as stated in *In re Best*, 562 F.2d 1252, 1255 (CCPA 1977),

> Where … the claimed and prior art products are identical or substantially identical, … the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product…. Whether the rejection is based on "inherency" under 35 U.S.C. § 102, on "prima facie obviousness" under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products.

An invention is obvious if "the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious . . . to a person having ordinary skill in the art to which said subject matter pertains." 35 U.S.C. § 103. The factual inquiries underlying obviousness include (1) the scope and content of the prior art, (2) the differences between the prior art and the claims at issue, (3) the level of ordinary skill in the art at the time the invention was made, and

(4) any objective evidence of non-obviousness. *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966).

"The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art." *In re Dow Chem. Co.*, 837 F.2d 469, 473 (Fed. Cir. 1988). In determining whether obviousness is established by combining the teachings of the prior art, "the test is what the combined teachings of the references would have suggested to those of ordinary skill in the art." *In re Keller,* 642 F.2d 413, 425 (CCPA 1981). Furthermore, in *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 415 (2007), the Supreme Court rejected a rigid application of a teaching-suggestion-motivation test in the obviousness determination. The Court emphasized that "the [obviousness] analysis need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418; *see also id.* at 421 ("A person of ordinary skill is . . . a person of ordinary creativity, not an automaton."). Thus, an "[e]xpress suggestion to substitute one equivalent for another need not be present to render such substitution obvious." *In re Fout*, 675 F.2d 297, 301 (CCPA 1982).

"Obviousness does not require absolute predictability of success. . . . [A]ll that is required is a reasonable expectation of success." *In re O'Farrell*, 853 F.2d 894, 903-04 (Fed. Cir. 1988). "[W]hen unexpected results are used as evidence of nonobviousness, the results must be shown to be unexpected

compared with the closest prior art." *In re Baxter-Travenol Labs.*, 952 F.2d 388, 392 (Fed. Cir. 1991).

B. Analysis

1. Rejection (A)

a. claim 1

The Examiner rejected claims 1-3, 15-17, 22-24, 26, and 38 as anticipated under § 102(b) by Nagai. Claim 1 is the sole independent claim on appeal. Claim 1 requires, in relevant part, a composition comprising "a therapeutically effective amount of at least one herbal active agent wherein the herbal active agent is selected from the group consisting of bioactive herbs, herbal extracts, tinctures, essential oils, and mixtures thereof." While Nagai describes oral mucosa-adhesive preparations containing a therapeutically effective amount of a medicament (FF 5), Nagai does not explicitly describe any medicament as a bioactive herb, herbal extract, tincture, and/or essential oil. Although the Examiner correctly found that Nagai's described medicaments include drugs such as digitalis and digoxin (FF 6), as pointed out by Appellants (Reply Br. 6-7; Surreply 7), these drugs may be prepared synthetically. Absent a sufficient factual basis establishing that any particular drug described by Nagai, such as digitalis, is inherently a herbal extract as claimed, we must reverse the rejection of claim 1 under § 102(b) over Nagai. Inherency cannot be established by probabilities or possibilities. For example, the mere fact that digitalis was originally isolated from plants of the genus *Digitalis* is insufficient to establish that the digitalis described in Nagai is a herbal extract as opposed to a synthetic drug.

Therefore, we reverse the rejection of claim 1, and claims 2-3, 15-17, 22-24, 26, and 38 dependent thereon, as anticipated under § 102(b) by Nagai.

2. Rejection (B)

a. claim 1

The Examiner rejected claims 1-4, 6, 15-17, 22-24, and 38 as anticipated under § 102(b) by Inoue. Claim 1, the sole independent claim on appeal, recites, in relevant part, a composition comprising "a pharmaceutically acceptable solid bioadhesive carrier, comprising a mucoadhesive synthetic polycarboxylic acid polymer, in an amount from about 40 to 99 percent based on the weight of the whole composition in a form suitable for administration and adhesion to the oral mucosa." Appellants argue that Inoue fails to meet this claim limitation.

Inoue describes a film composition for administering an active ingredient, e.g., Lithospermi Radix extract, incorporated into a compatible mixture of polycarboxylic acids and polyvinyl acetate, to the oral mucosa (FF 8, 13, and 17). Appellants argue that polyvinyl acetate is nondegradable and, therefore, Inoue's films must be removed from the mouth after the active ingredient has been released (Surreply 3-4). We understand Appellants to argue that Inoue does not describe a bioadhesive as claimed. However, this argument is not commensurate in scope with claim 1 and, therefore, is not persuasive.

According to the 413 Specification, a bioadhesive is an adhesive which attaches to mucosal tissue upon hydration, which maintains adhesion in moist or wet *in vivo* environments, and which attaches to the oral mucosa without the need for reinforcement by means of another adhesive which is applied to a backing (FF 1). Inoue's bioadhesive is a carefully defined "compatible" mixture of polycarboxylic acids and polyvinyl acetate formed into a thin and soft film which exerts strong adhesion to the wet oral mucosa

for an extended period of time (FF 8-9). Inoue's bioadhesive film attaches to the oral mucosa without the need for reinforcement (FF 15). Thus, Inoue's bioadhesive film is a bioadhesive as defined in the 413 Specification.

Appellants also argue that Inoue's bioadhesive carrier film is not present in the required amount of about 40 to 99% by weight of the total composition. However, as found by the Examiner (Ans. 12-13; Supp. Ans.[12] 13), Inoue discloses that the amount of drug incorporated usually ranges from 0.0001 to 35% by weight based on the weight of the composition (FF 18). Thus, the Examiner reasoned that Inoue's composition contained an amount of bioadhesive carrier within the claimed range. We agree with the Examiner that there is a sufficient factual basis for reasonably believing that the composition of Inoue is the same or substantially the same as the claimed composition and Appellants have not shown otherwise. *In re Best*, 562 F.2d at 1255.

At best, Appellants argue that Inoue's composition may contain other additives, e.g., neutralizing substances, and residual solvent from casting the film, as well as a support film of unknown weight (App. Br. 7; Reply Br. 3). However, Inoue teaches that such additives and support films are optional (FF 10 and 15) and Appellants have not shown that residual solvent from casting would have reduced the amount of bioadhesive carrier in Inoue's composition to less than 40% by weight.

Therefore, we agree with the Examiner that the subject matter of claim 1 is described by Inoue. Since claims 4, 6, 15-17, 23, and 24 have not been separately argued by Appellants, we sustain the rejection of claims 1, 4, 6, 15-17, 23, and 24 under § 102(b) as anticipated by Inoue.

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[12] Examiner's Answer mailed 29 August 2007 ("Supp. Ans.").

b. claims 2 and 38

Appellants further argue that Inoue fails to describe a composition in the form of a disc having the diameters and thicknesses recited in claims 2 and 3. Specifically, claims 2 and 3 recite thicknesses of 0.4 to 2.3 mm and 1 to 2 mm, respectively. Inoue describes compositions with bioadhesive carrier films having thicknesses of from 5 to 100 µm, i.e., from 0.005 to 0.1 mm (FF 14). Assuming *arguendo* that Inoue's composition further comprised a support film, Inoue describes support films as having a thickness from 10 to 100 µm, i.e., from 0.010 to 0.100 mm (FF 16). Thus, while Inoue describes compositions with thicknesses of at least 5 µm as argued by the Examiner, Inoue does not explicitly describe compositions with thicknesses of at least 0.4 mm. Moreover, the Examiner has not established a sufficient factual basis for finding that Inoue inherently describes compositions with a thickness of at least 0.4 mm. Rather, it reasonably appears that Inoue probably suggests compositions with thicknesses about 0.2 mm (*see* FF 14 and 16). Similarly, the Examiner directs our attention to column 8, lines 45-61, of Inoue for a description of a composition having a diameter from 5 mm to 20 mm (Ans. 14; Supp. Ans. 14). However, as noted by Appellants (*see e.g.,* Surreply 5), we find no such disclosure at that cite.

Therefore, we agree with Appellants that the subject matter of claims 2, 3, and 38 is not described by Inoue.

c. claim 22

Finally, Appellants argue that Inoue fails to describe a bioadhesive carrier comprising crosslinked polycarboxylic acids (claim 22). As pointed out by the Examiner (Ans. 14; Supp. Ans. 14), Inoue describes neutralizing

polycarboxylic acids with metal salts, e.g., zinc oxide (FF 10). The Examiner maintains that the neutralization reaction will inherently cause the polycarboxylic acids to crosslink as evidenced by Odian (Ans. 14-15; Supp. Ans. 14-15). However, as noted by Appellants (Reply Br. 5-6; Surreply 5-6), Odian teaches that neutralizing poly(meth)acrylic acids (i.e., polycarboxylic acids) with metal salts, e.g., zinc oxide, yields ionomers which *behave* like crosslinked thermoplastics as a result of microphase separation, not that the neutralization causes physical crosslinking *per se* as asserted by the Examiner (FF 29).

Therefore, we agree with Appellants that the subject matter of claim 22 is not described by Inoue.

To summarize, we sustain the rejection of claims 1, 4, 6, 15-17, 23, and 24 under § 102(b) as anticipated by Inoue, but reverse the rejection of claims 2, 3, 22, and 38.

3. Rejection (C)

The Examiner rejected claims 1-4, 6-12, 15-17, 19, 22-24, and 38 as obvious under § 103(a) over Inoue in view of Iyer and Friedman, as evidenced by Lawless.

a. claim 1

We have found claims 1, 4, 6, 15-17, 23, and 24 anticipated by Inoue under § 102(b). Since anticipation is the ultimate of obviousness, the subject matter of these claims is necessarily obvious and we need not consider them further. Thus, we sustain the rejection of claims 1, 4, 6, 15-17, 23 and 24 under § 103(a) as obvious over Inoue in view of Iyer and Friedman. *In re Fracalossi*, 681 F.2d 792, 794 (CCPA 1982).

b. claims 2, 22, and 38

The Examiner has not provided an alternative obviousness analysis for the subject matter of claims 2, 3, 22, and 38 over the combined teachings of Inoue, Iyer, and Friedman. Therefore, we summarily reverse the rejection of claims 2, 3, 22, and 38 under § 103(a) as obvious over the combined teachings of Inoue, Iyer, and Friedman.

c. claims 7, 12, and 19

Appellants argue that claims 7-12 and 19 are unobvious because none of the applied references teach or suggest a composition comprising a bioadhesive carrier in amount of about 40 to 99 weight% based on the total weight of the composition as required by claim 1. This argument is not persuasive because we find claim 1 anticipated by Inoue for the reasons given above.

i. claims 12 and 19

Appellants further argue that Inoue fails to teach or suggest a composition comprising $MgBr_2$, NaCl, and/or KCl as required by claim 12 or a composition containing carnallite or a salt thereof as required by claim 19 (App. Br. 15). We do not find, and the Examiner has not indicated, where Inoue, Iyer, and/or Friedman or any other evidence of record teach or suggest the limitations of claims 12 and 19. Therefore, we reverse the rejection of claims 12 and 19 as obvious under § 103(a) over the combined teachings of Inoue, Iyer, and Friedman.

ii. claim 7

Appellants also argue that there is no motivation to combine the teachings of the applied references (App. Br. 14; Reply Br. 13). In particular, Appellants argue that one of ordinary skill in the art would not have been motivated to combine the non-bioadhesive formulations of Iyer, Friedman,

and Lawless with the bioadhesive formation of Inoue (App. Br. 16). This argument is not persuasive.

Here, Iyer teaches using a combination of herbal active agents, including cedarwood oil, citronella oil, lemon oil, and/or *Glycyrrhiza glabra* (licorice root) extract for topical application to the oral mucosa to inhibit or prevent bacterial growth (FF 19-23). Similarly, Friedman teaches using specific combinations of essential oils, such as cinnamon oil, citronella oil, lemon oil, and tea-tree oil, and herbal extracts, such as Glycerrhiza extracts, for topical application to the oral mucosa to treat microbial infections caused by bacteria or fungi (FF 24-26). As evidenced by Lawless, lemon oil contains approximately 70% limonene, with the remainder comprising terpinene, pinenes, myrcene, and sabinene (FF 28). Iyer and Friedman both teach topical application of their formulations directly to oral surfaces (FF 19-20 and 24), albeit not in a formulation comprising a bioadhesive carrier film as taught by Inoue. However, Inoue teaches and/or suggests administering active agents, such as plant extracts, to oral mucosal surfaces (FF 9, 17). The test for determining obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art. *In re Keller*, 642 F.2d at 425. Here, we agree with the Examiner that Iyer and Friedman suggests incorporating a combination of herbal active agents, including at least an essential oil, such as lemon oil, into Inoue's "oral bandage," a composition known to be useful for topical administration of drugs, including herbal active agents, to the oral mucosal cavity, to inhibit or prevent undesired microbial growth in the mouth. Therefore, this argument is not persuasive.

Consequently, we sustain the rejection of claims 7-11 under § 103 over the combined teachings of Inoue, Iyer, and Friedman, as evidenced by Lawless.

d. claims 1 and 7

Appellants additionally argue that the claimed invention provides unexpected results (Surreply 16-17). Specifically, Appellants contend that Examples 4 and 6 of the 413 Specification illustrate unexpected efficacy of the claimed compositions vis-à-vis the films described in Inoue (*id.*). The tablets of Example 4 were prepared by compression molding of herbal active compositions in powder form and mixtures of Carbopol 940, HPMC, and other ingredients, such as magnesium stearate (*see e.g.,* Spec. 29-31). None of the claimed compositions are limited to compression molded tablets formed from mixtures of Carbopol 940 and HPMC or require magnesium stearate. Similarly, Example 6 of the 413 Specification describes treating 17 patients with recurrent aphthous stomatitis with compositions loaded with carnallite, citron oil, and benzocaine. None of the claimed compositions are limited to the compositions described in Example 6 of the 413 Specification. Furthermore, no direct comparison was made with the compositions of Inoue, e.g., using the same active ingredients on the same 17 patients. Thus, Appellants' proffered showing of unexpected results is neither commensurate in scope with the claimed invention nor a comparison with the closest prior art. Therefore, this showing is insufficient evidence of nonobviousness.

To summarize, we sustain the rejection of claims 1, 4, 6-11, 15-17, 23, and 24 under § 103 over Inoue, Iyer, and Friedman, as evidenced by Lawless, but reverse the rejection of claims 2, 3, 12, 19, 22, and 38.

C. Conclusion

The rejection of claims 1-3, 15-17, 22-24, 26, and 38 under § 102 over Nagai is reversed because Nagai does not describe a composition comprising a bioactive herb, a herbal extract, a tincture, and/or an essential oil.

The rejection of claims 1, 4, 6, 15-17, 23, and 24 under § 102 over Inoue is sustained because the evidence of record supports the finding that Inoue describes a composition comprising a bioadhesive carrier in an amount of about 40 to 99 wt. % based on the total weight of the composition. However, the rejection of claims 2, 3, 22, and 38 under § 102 over Inoue is reversed because the evidence of record fails to support a finding that Inoue describes compositions having the claimed diameters, thicknesses, surface area, or crosslinked polymers.

The rejection of claims 1, 4, 6, 15-17, 23, and 24 under § 103 over Inoue, Iyer, and Friedman as evidenced by Lawless is sustained because the evidence of record supports the finding that Inoue describes a composition comprising a bioadhesive carrier in an amount of about 40 to 99 wt. % based on the total weight of the composition. However, the rejection of claims 2, 3, 12, 19, 22, and 38 under § 103 over Inoue, Iyer, and Freidman as evidenced by Lawless is reversed because the evidence of record fails to support a finding that Inoue describes compositions having the claimed diameters, thicknesses, surface area, crosslinked polymers, or additional ingredients, i.e., $MgBr_2$, NaCl, KCl, carnallite or a salt thereof.

Claims 14, 20, 21, and 25 have not been rejected by the Examiner.

IV. Order

Upon consideration of the record, and for the reasons given, it is

ORDERED that the decision of the Examiner to reject claims 1-3, 15-17, 22-24, 26, and 38 as anticipated under § 102 by Nagai is REVERSED;

FURTHER ORDERED that the decision of the Examiner to reject claims 1, 4, 6, 15-17, 23, and 24 as anticipated under § 102 by Inoue is AFFIRMED;

FURTHER ORDERED that the decision of the Examiner to reject claims 2, 3, 22, and 38 as anticipated under § 102 by Inoue is REVERSED;

FURTHER ORDERED that the decision of the Examiner to reject claims 1, 4, 6-11, 15-17, 23, and 24 as obvious under § 103 over the combined teachings of Inoue, Iyer, and Friedman, as evidenced by Lawless, is AFFIRMED,

FURTHER ORDERED that the decision of the Examiner to reject claims 2, 3, 12, 19, 22, and 38 as obvious under § 103 over the combined teachings of Inoue, Iyer, and Friedman, as evidenced by Lawless, is REVERSED, and

FURTHER ORDERED that no that no time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

cdc

PATREA L. PABST
PABST PATENT GROUP LLP
400 COLONY SQUARE, SUITE 1200
1201 PEACHTREE STREET
ATLANTA, GA 30361